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Subject: Axicabtagene Ciloleucel (Yescarta) Infusion

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Axicabtagene ciloleucel (Yescarta) is a CD19-directed, genetically-modified autologous T cell immunotherapy that was first approved by the U.S. Food and Drug Administration (FDA) in October 2017 for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. Axicabtagene ciloleucel was previously granted orphan designation by the FDA for the treatment of DLBCL in March 2014. Axicabtagene ciloleucel works by reprogramming a patient's own T cells with a transgene encoding a chimeric antigen receptor (CAR) to identify and eliminate CD19-expressing malignant and normal B cells. Treatment involves removing, genetically modifying, and then re-infusing a patient's own T-cells. Axicabtagene ciloleucel is the second CAR T-cell therapy to be approved by the FDA. The first CAR T-cell therapy was tisagenlecleucel (Kymriah) approved by the FDA in August 2017 for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

Diffuse large B-cell lymphomas are the most common lymphoid neoplasms in adults, and account for approximately 32.5% of non-Hodgkin lymphoma (NHLs) cases diagnosed annually. The DLBCLs exhibits large heterogeneity in morphologic, genetic, and clinical aspects. Multiple clinicopathologic entities are defined by the 2016 World Health Organization (WHO) classification, which are sufficiently distinct to be considered separate diagnostic categories. Adequate immunophenotyping is essential to establish the diagnosis, and to determine germinal center B-cell like (GCB) vs. non-GBC origin. Combination chemoimmunotherapy in the first-line setting (e.g., rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone [R-CHOP]) is associated with a 5-year survival rate ranging from 60% to 70%. Interim restaging should be performed to identify patients who disease has not responded to or has

progressed on induction therapy. Based on a number of prognostic factors, 20% to 50% of DLBCL cases are refractory or relapse after first-line chemotherapy and the response rates to subsequent salvage chemotherapy and consolidation with autologous hematopoietic stem cell transplantation (HSCT) is suboptimal. The National Comprehensive Cancer Network (NCCN) B-cell Lymphoma Guidelines (Version 1.2019) list axicabtagene ciloleucel as a category 2A recommendation for the treatment of relapsed/refractory DLBLC, primary mediastinal large B-cell lymphoma (PMBCL), high-grade B-cell lymphoma [with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma), or not otherwise specified (NOS)], AIDS-related DLBCL, HHV8-positive DLBCL, NOS, and monomorphic post-transplant lymphoproliferative disorders (PTLD) (B-cell type) for patients with two or more disease relapses (if not previously given), or, for those patient with the intention to proceed to high-dose therapy, a non-complete response (i.e., partial response or worse) to second-line therapy. Axicabtagene ciloleucel is also a 2A recommendation for the treatment of follicular lymphoma with histological transformation to DLBCL in patients with 2 or more prior chemotherapy regimens (with at least one being an anthracycline or anthracenedione-based regimen, unless contraindicated).

The safety and efficacy of axicabtagene ciloleucel leading to FDA approval was based on the results of an single-arm, open-label, multicenter phase 1/2 study called ZUMA-1, which reported complete remission (CR) rates and duration of response demonstrated in the phase 2 portion of the study. Adults (≥18 years of age) with aggressive B-cell NHL (which included DLBCL, primary mediastinal B-cell lymphoma, and transformed follicular lymphoma according to the 2008 WHO classification system) that was primary refractory, refractory to a second or greater line of therapy, or relapsed within 1 year after autologous hematopoietic stem cell transplantation (HSCT) were enrolled in the study. The study excluded patients with prior allogeneic HSCT, any history of CNS lymphoma, ECOG performance status of 2 or greater, absolute lymphocyte count less than 100/µL, creatinine clearance less than 60 mL/min, hepatic transaminases more than 2.5 times the upper limit of normal, cardiac ejection fraction less than 50%, or active serious infection. Of the patients treated, the median age was 58 years (range: 23 to 76), 67% were male, and 89% were white. Most (76%) had DLBCL, 16% had transformed follicular lymphoma, and 8% had primary mediastinal large B-cell lymphoma. The median number of prior therapies was 3 (range: 1 to 10), 77% of the patients had refractory disease to a second or greater line of therapy, and 21% had relapsed within 1 year of autologous HSCT. Only two patients received axicabtagene ciloleucel after failure of one prior line of therapy. All patients received a lymphodepleting regimen of cyclophosphamide and fludarabine prior to infusion of axicabtagene ciloleucel. Of the 111 patients who underwent leukapheresis, 101 received the infusion (9 were not treated due to progressive disease or serious adverse reactions following leukapheresis and there was a manufacturing failure in 1 patient). Study protocol mandated hospitalization of patients for infusion and 7 days after infusion. Bridging chemotherapy between leukapheresis and lymphodepleting chemotherapy was not permitted. The median time from leukapheresis to product delivery was 17 days (range, 14 to 51 days). The primary end point is objective response rate (ORR) as assessed by an independent review committee (IRC) according to the International Working Group (IWG) Response Criteria for Malignant Lymphoma (see “Other” section) based on a modified intention-to-treat population of all patients who has received axicabtagene ciloleucel. The main secondary endpoint is the duration of response (DOR) that was censored for HSCT in remission. The median follow up for DOR was 7.9 months. Results are summarized in Table 1. The evaluation of DOR remains limited by the large amount of censoring before 6 months.

Table 1: Results of ZUMA-1 as Assessed by the Independent Review Committee

Outcome	Results, n (%) (95% Confidence Interval)
Primary end point (n=101)	

Objective response rate (CR + PR)	73 (72%) (62 to 81%)
CR	52 (51%) (41 to 62%)
PR	21 (21%) (13 to 30%)
SD	19 (19%)
PD	7 (7%)
Not evaluable	2 (2%)
Secondary end points	
Median duration of response (n=73)	
All patients	9.2 months (5.4 to NE)
CR only	NE (8.1 to NE)
PR only	2.1 months (1.3 to 5.3)
CR: complete response; NE: not estimable; PD: progressive disease; PR: partial response; SD: stable disease	

Safety data assessed 108 patients treated with axicabtagene ciloleucel. Adverse events of special interest are summarized in Table 2. All patients experienced at least one adverse event following infusion and 94% (n=102) experienced grade 3 or higher events. Serious adverse events were observed in 56 (52%) of patients, and serious adverse events that were grade 3 or higher occurred in 48 (44%) patients. Overall, 34 deaths were reported from the time of informed consent to the trial data cutoff (January 27, 2017). Thirty patients died of progressive disease and 4 deaths were attributed to axicabtagene ciloleucel as per FDA analysis, of which 3 occurred within 30 days of infusion. The median time to onset for cytokine release syndrome (CRS) was 2 days (range, 1 to 12 days), and the median time to resolution was 7 days (range for CRS duration, 2 to 58 days). Forty-five percent (49/108) of patients received tocilizumab for CRS management. The median time to onset of neurologic toxicity was 4 days (range, 1 to 43 days). The median duration was 17 days. The most common neurologic toxicities included encephalopathy, headache, tremor, dizziness, aphasia, delirium, insomnia, and anxiety. Ninety-eight percent (98%) of all neurologic toxicities occurred within first 8 weeks of axicabtagene ciloleucel infusion.

Table 2: Summary of Key Serious Adverse Events in ZUMA-1 (n=108)

Adverse Event	All Grades, n (%)	Grades ≥3, n (%)
Cytokine release syndrome	101 (63%)	14 (13%)
Neurologic toxicities	94 (21%)	34 (31%)
Serious infections	41 (38%)	25 (23%)
Febrile neutropenia	39 (36%)	35 (32%)
Prolonged cytopenia not resolved by day 30	--	30 (28%)
Hypogammaglobulinemia	16 (15%)	0

POSITION STATEMENT:

Administration of axicabtagene ciloleucel (Yescarta) **meets the definition of medical necessity** when **ALL** of the following criteria are met (“1” to “10”):

1. Member will be 18 years of age or older at the time of the treatment infusion
2. Member has a diagnosis of large B-cell lymphoma that includes any of the following subtypes (“a” to “h”)- documentation of the lymph node biopsy results **AND** immunophenotyping and/or gene expression profiling results with interpretation confirming the diagnosis and specific subtype must be submitted:
    a. Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS)
    b. Primary mediastinal large B-cell lymphoma (PMBCL or PMBL)

c. High-grade B-cell lymphoma (HGBL), with *MYC* and *BCL2* and/or *BCL6* translocations [a.k.a., double-hit or triple-hit lymphomas]

d. High-grade B-cell lymphoma, NOS

e. DLBCL arising from follicular lymphoma [a.k.a., follicular lymphoma with histological transformation to DLBCL or transformed follicular lymphoma (TFL)]

f. AIDS-related diffuse large B-cell lymphoma

g. HHV8 (human herpesvirus 8)-positive diffuse large B-cell lymphoma, NOS

h. Monomorphic post-transplant lymphoproliferative disorders (PTLD) (B-cell type)

3. Member has relapsed or refractory disease meeting **EITHER** of the following criteria ("a" or "b"):
   a. Member was unable to achieve a complete response (CR) following their second line of systemic chemotherapy
   b. Member's disease is in second or greater relapse/recurrence
4. Member has received **TWO** or more unique lines of systemic chemotherapy for their disease (which may or may not include therapy supported by autologous stem cell transplant), **AND** prior therapy must have included an anti-CD20 monoclonal antibody (e.g., rituximab) unless the tumor is CD20 negative or the member has an FDA-labeled contraindication to anti-CD20 therapy – medical record documentation of the member's prior lines of therapy for their lymphoma must be submitted
5. Following the completion of lymphodepleting chemotherapy (as needed), axicabtagene ciloleucel will be used as single-agent therapy (i.e., not used in combination with maintenance chemotherapy)
6. Member has adequate organ and bone marrow function with no significant deterioration expected within 4 weeks after apheresis as determined by the treating oncologist/hematologist
7. Axicabtagene ciloleucel will not be administered if the member has an uncontrolled systemic infection at the time of planned treatment initiation
8. Member has **NOT** previously received CD19-directed chimeric antigen receptor (CAR) T-cell therapy (including axicabtagene ciloleucel) in their lifetime for the treatment of lymphoma or leukemia
9. The healthcare facility where axicabtagene ciloleucel is to be administered has enrolled in the Yescarta REMS program
10. The administration of axicabtagene ciloleucel will not exceed one single dose as provided by the manufacturer

Approval duration: 3 months to allow for a one-time infusion of therapy

Axicabtagene ciloleucel (Yescarta) is considered **experimental or investigational** for all other indications, including but not limited to the following, due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcomes:

- All non-lymphoma malignancies
- Burkitt lymphoma/leukemia (i.e., patients with mature B-cell ALL)
- Castleman's disease
- Lymphoblastic lymphoma
- Mantle cell lymphoma
- Marginal zone lymphomas
- Non-B-cell lymphomas (e.g., T-cell lymphomas)

- Non-transformed follicular lymphoma
- Primary cutaneous B-cell lymphomas
- Primary DLBCL of the central nervous system (CNS)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.
- Limitation of Use: axicabtagene ciloleucel is not indicated for the treatment of patients with primary central nervous system lymphoma.
- Each single infusion bag contains a suspension of chimeric antigen receptor (CAR)-positive T cells in approximately 68 mL. The target dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells, to be infused within 30 minutes. Do NOT use a leukodepleting filter, and premedicate with acetaminophen and an H1-antihistamine.
- Administer a lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m^2 intravenously and fludarabine 30 mg/m^2 intravenously on the fifth, fourth, and third day before infusion of axicabtagene ciloleucel.
- Tocilizumab and emergency equipment should be available prior to infusion and during the recovery period.
- Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS and neurologic toxicities. The product labeling gives specific treatment recommendations for the different grades of CRS and neurologic toxicity. Instruct patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.
- For further information on the preparation, administration, and monitoring of axicabtagene ciloleucel can be found in the product labeling.

Dose Adjustments

- Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.
- Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability

- Supplied in an infusion bag containing approximately 68 mL of frozen suspension of genetically modified autologous T cells in 5% DMSO and 2.5% albumin (human). Each infusion bag is individually packed in a metal cassette. Axicabtagene ciloleucel is stored in the vapor phase of liquid nitrogen and supplied in a liquid nitrogen dry shipper.

PRECAUTIONS:

Boxed Warning

- WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES
    - Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving axicabtagene ciloleucel. Do not administer axicabtagene ciloleucel to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
    - Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving axicabtagene ciloleucel, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with YESCARTA. Provide supportive care and/or corticosteroids as needed.
    - Axicabtagene ciloleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA REMS.

Contraindications

- None

Precautions/Warnings

- **Cytokine Release Syndrome (CRS):** CRS, including fatal or life-threatening reactions, occurred following treatment. Among patients who died after receiving axicabtagene ciloleucel, four had ongoing CRS events at the time of death. Key manifestations of CRS include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (20%). Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS). Ensure that 2 doses of tocilizumab are available prior to infusion. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for 4 weeks after infusion. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.
- **Neurologic Toxicities**: Neurologic toxicities, that were fatal or life-threatening, occurred following treatment. Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicities. Monitor patients for signs or symptoms of neurologic toxicities for 4 weeks after infusion and treat promptly.
- **YESCARTA REMS**: Because of the risk of CRS and neurologic toxicities, axicabtagene ciloleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA REMS. The required components of the YESCARTA REMS are:
    - Healthcare facilities that dispense and administer axicabtagene ciloleucel must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within 2 hours after infusion, if needed for treatment of CRS.
    - Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense or administer axicabtagene ciloleucel are trained about the management of CRS and neurologic toxicities.

      Further information is available at www.YescartaREMS.com or 1-844-454-KITE (5483).
- **Hypersensitivity Reactions**: Allergic reactions may occur with the infusion of axicabtagene ciloleucel. Serious hypersensitivity reactions including anaphylaxis may be due to dimethyl sulfoxide (DMSO) or residual gentamicin. Monitor for hypersensitivity reactions during infusion.

- **Serious Infections**: Severe or life-threatening infections occurred in patients after infusion. Monitor patients for signs and symptoms of infection before and after infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids and other supportive care as medically indicated.
- **Prolonged Cytopenias**: Patients may exhibit Grade 3 or higher cytopenias for several weeks following infusion. Monitor complete blood counts.
- **Hypogammaglobulinemia**: B-cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment. Monitor immunoglobulin levels after treatment and manage using infection precautions, antibiotic prophylaxis, and immunoglobulin replacement as needed.
- **Secondary Malignancies**: Patients may develop secondary malignancies. Monitor the patient life-long for secondary malignancies. In the event that a secondary malignancy occurs after treatment, contact Kite at 1-844-454-KITE (5483).
- **Effects on Ability to Drive and Use Machines**: Due to the potential for neurologic events, including altered mental status or seizures, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery during this time period.

BILLING/CODING INFORMATION:

The collection of leukapheresis provides the starting material for the manufacturing of axicabtagene ciloleucel and should **NOT** be billed separately.

HCPCS Coding

Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

ICD-10 Diagnoses Codes That Support Medical Necessity

C83.30 - C83.39	Diffuse large B-cell lymphoma
C85.10 - C85.19	Unspecified B-cell lymphoma
C85.20 - C85.29	Mediastinal (thymic) large B-cell lymphoma
C85.80 - C85.89	Other specified types of non-Hodgkin lymphoma
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

DEFINITIONS:

Autologous: Cells or tissues obtained from the same individual (as opposed to from a different person).

CD19: Cluster of Differentiation 19 is a protein found on the surface of B-cells in humans. Fully differentiated plasma cells no longer express CD19.

Chimeric antigen receptor (CAR) T-cell therapy: A type of treatment in which a patient's T cells are changed in the laboratory so they will attack cancer cells. T cells are taken from a patient's blood. Then the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added in the laboratory. The special receptor is called a chimeric antigen receptor (CAR). Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion.

Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS): The 2008 WHO classification of mature B-cell lymphomas included DLBCL, NOS as a new category to include germinal center B-cell (GCB) subtype, activated B-cell (ABC) subtype as well as other DLBCL cases that do not belong to any of the four specific subtypes (T-cell/histiocyte rich large B-cell lymphoma, primary CNS DLBCL, primary cutaneus DLBCL ("leg type"), or EBV+ DLBCL of the elderly). The updated 2016 WHO classification system created additional categories that fall outside of the definition of DLBCL, NOS.

Gene therapy: The therapeutic delivery of nucleic acid polymers into a patient's cells as a drug to treat disease.

Leukapheresis: A laboratory procedure in which white blood cells (WBC) are separated from a sample of blood. It is a specific type of apheresis, the more general term for separating out one particular constituent of blood and returning the remainder to the circulation. It is the first step in CAR T-cell therapy.

Primary mediastinal large B-cell lymphoma (PMBL): A distinct subtype of NHL presenting with primary site of disease in the mediastinum with or without other site and has histology of DLBCL. It tends to occur in young adults with a median age of 35 years with a slight female predominance.

RELATED GUIDELINES:

Adoptive Immunotherapy, 01-96400-01
Tisagenlecleucel (Kymriah) Infusion, 09-J2000-91

OTHER:

Eastern Cooperative Oncology Group (ECOG) Performance Status

Grade	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair

International Working Group (IWG) Response Criteria for Malignant Lymphoma

Response	Definition	Nodal Masses	Spleen, Liver	Bone Marrow
Complete remission (CR)	Disappearance of all evidence of disease	(a) FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative (b) Variably FDG-avid or PET negative; regression to normal size on CT	Not palpable, nodules disappeared	Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immuno-histochemistry should be negative
Partial remission (PR)	Regression of measurable disease and no new sites	≥50% decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes (a) FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site (b) Variably FDG-avid or PET negative; regression on CT	≥50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen	
Stable disease (SD)	Failure to attain CR/PR or PD	(a) FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET (b) Variably FDG-avid or PET negative; no change in size of previous lesions on CT		
Relapsed disease or progressive disease (PD)	Any new lesion or increase by ≥50% of previously involved sites from nadir	Appearance of a new lesion(s) >1.5 cm in any axis, ≥50% increase in SPD of more than one node, or ≥50% increase in longest diameter of a previously identified node >1 cm in short axis Lesions PET positive if FDG-avid lymphoma or PET positive prior to therapy	>50% increase from nadir in the SPD of any previous lesions	New or recurrent involvement

FDG - [^{18}F]fluorodeoxyglucose; PET - positron emission tomography; CT - computed tomography; SPD - sum of the product of the diameters

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/09/19.

GUIDELINE UPDATE INFORMATION:

03/15/18	New Medical Coverage Guideline.
04/01/18	Addition of HCPCS code Q2041 and deletion of J9999.
04/10/18	Revision to Billing and Coding section.
07/15/18	Revision to guideline consisting of updating the position statement.
01/01/19	Revision: HCPCS code updates. Modified Q2041 description.
02/15/19	Review and revision of guidelines consisting of updating the description, position statement, billing/coding, related guidelines, and references.